Medicines & Healthcare products Regulatory Agency

MHRA

MHRA regulatory centre and Research Ethics Service (RES) Combined Ways of Working Pilot

Instructions to Sponsors (Version 3.7)

NHS Health Research Authority

Document purpose:

The purpose of this document is to provide instructions to sponsors participating in the MHRA regulatory centre and RES Combined Ways of Working Pilot.

Please note that under the Combined Ways of Working pilot, a single application is submitted by the Sponsor or Contract Research Organisation. This is considered to be on behalf of the Chief Investigator for Research Ethics Committee submission.

Process:

STEP 1: Register your trial application

Contact cwow@hra.nhs.uk
You will need to provide the following details (where possible):
Trial title
IRAS ID
EudraCT number
Phase of the trial
If it is an ATIMP trial
Is the trial taking place in the NHS/HSC
Which UK nation the trial is led from (trials taking place in the NHS/HSC only)
Name and contact details of the sponsor
Whether the trial is going through HRA radiation assurance
Whether the trial is going through pharmacy assurance
Approximate submission date

STEP 2: Confirm your submission date

When you are confident that you will be able to submit your application within a particular time period (REC meeting submission period), please contact cwow@hra.nhs.uk to confirm your readiness.

Committee meeting dates and submission periods can be found here. If you have a REC preference, this should be detailed in your email

There will be a small number of RECs involved in this pilot during the early stage. This means that you may not be able to submit to the REC which you would usually submit to. The RECs involved will increase as the pilot develops so please always check the HRA website for the most up to date information.

Once you have confirmed your submission and the application has been allocated to a REC meeting you will be issued with a REC reference number.

STEP 3: Submit application

All applications which are submitted under the CWoW pilot must be submitted via the new part of IRAS https://www.myresearchproject.org.uk/CWOW/

For details of how to make a submission, please refer to IRAS for CWoW step-by-step instructions

NOTE: If you will not complete the above process by the date agreed in Step 1, contact cwow@hra.nhs.uk to rearrange your REC review as soon as possible.

STEP 4: Validation Process

Validation checks will be completed on your application within 3 days of receipt. This will involve checking that all required documents have been submitted and that the documents can be opened and are readable. If the application is not valid, you will be given the opportunity to correct this and will have until day 'Submission+5' to complete. The validation check will be undertaken by the MHRA.

For further information on which documents are required, please refer to the Application Dossier Guidance which can be found here.

Not all documents in the document checklist table (Appendix) may be appropriate for all trials. Where a document listed in the table is not submitted because it is not relevant or because the information is contained elsewhere in the application dossier, such as in the protocol, then you just need to detail this in the comments column for the purposes of validation.

When naming documents to be submitted, the full title may be listed in the cover letter but the naming of the document when saving it should be a short but clear version.

Day 0 will be the date of receipt of a valid application.

STEP 5: consolidated assessment; to be completed by day 30

MHRA and REC will work jointly to undertake the assessment which will result in two assessment outputs. Assessment one will include the full MHRA review and also a review by the REC of the risks, benefits, burdens and inconveniences. (Note that CMC-related information will be assessed by the MHRA only). Assessment 2 will be the REC review (other than the areas covered in assessment 1) and an administrative assessment, which is largely in relation to compliance with legislation (e.g data and tissue legislation).

The output at this stage of the process will either be an overall authorisation of the trial (CTA from MHRA and favourable opinion from the ethics committee) or a request for further information.

STEP 6: Request for further information

If we require further information, you will receive notification via the dashboard and also the person named on the EudraCT form as the sponsor contact will receive an email.
This will outline the further information required or the questions to be answered. This will include all points which need to be responded to as part of the co-ordinated review. Please note, it is the responsibility of the sponsor organisation to ensure that the appropriate person or persons within the organisation receive the request for further information. Generic rather than personal email addresses are strongly advised.

STEP 7: Request for further information response

You will have 14 days to provide a full response.

The response should be submitted via IRAS.

NOTE: We anticipate that there may be instances where you cannot respond in full to the requests for information. The UK clinical trials Regulation 2004 No SI1031 allows a fixed period of time, usually 14 days, to respond to a request for further information in relation to the CTA whereas the Regulation allows for the clock to be paused while awaiting a response to the REC. Therefore, if you are unable to respond in full to the request for further information (including assessments 1 and 2) within 14 days please contact the CWoW admin (cwow@hra.nhs.uk) mailbox urgently to discuss whether an extension can be given.

STEP 8: Joint Decision; by day 60*

*For ATIMP trial applications we work towards the statutory timeline of 90 days (which may be extended to 180 days where a specialist committee is consulted). However, we will aim to issue the final decision within 60 days as per other CTIMP applications.

After the review of a full response to all points raised (assessment 1 and 2), an outcome will be confirmed (authorised or not authorised). Confirmation will be via the dashboard in the system and additionally, two letters will be issued via e-mail.

An authorisation will be issued where the CTA is authorised and also the REC has issued a favourable opinion and will include both the CTA authorisation letter and the REC favourable opinion letter.
A non-authorisation will occur because either the CTA has been rejected or the REC has issued an unfavourable opinion. The CTA and REC letters will both be provided and the reason for the non-authorisation will be made clear.

Additionally, for trials taking place in the NHS/HSC and led from sites in England and Wales, an additional letter confirming the HRA & HCRW Approval status will also be provided (subject to all authorisations being in place). For trials led by sites in Scotland and Northern Ireland, the combined process will involve co-ordination with the study wide review but the outcome will be issued separately.

Fortnightly Support and Feedback Call:

The purpose of the trial is to test a joint MHRA/RES process; this includes understanding the experience of applicants. As such, we want to ensure continued engagement with you throughout, to help you with any areas of need but also to ensure we're capturing your experience and feedback in a consistent and usable way.

To support this, we will host a fortnightly call where we'll be on hand to help you with any areas and to ask you questions about your progress.

Whilst our preference is for matters to be raised during this weekly call, we will of course be on hand should you have needs that don't fit the scheduled call timeline.

The meeting will run alternate **Mondays at 14:00** (to confirm the date of the next call please e-mail cwow@hra.nhs.uk)

Trials excluded from this stage of the pilot:

- Trials requiring review by the REC constituted by Scottish Ministers under Section 51(6) of the Adults with Incapacity Act 2006.

Further information

Further information and guidance will be issued via the Combined Ways of Working Pilot page on the HRA website which can be found here .

Appendix 1

Table 1 – Checklist (To be copied into the cover letter)

Information	Present (Y/N/NA)	Comment
1. COVER LETTER		
2. IRAS EudraCT form : PDF and XML file		
3. PROTOCOL		
4. INVESTIGATOR'S BROCHURE (IB)		
5. DOCUMENTATION RELATING TO COMPLIANCE WITH GOOD MANUFACTURING PRACTICE (GMP) FOR THE INVESTIGATIONAL MEDICINAL PRODUCT		
6. INVESTIGATIONAL MEDICINAL PRODUCT DOSSIER (IMPD)		
7. AUXILIARY (ie non-IMP) MEDICINAL PRODUCT DOSSIER		
8. SCIENTIFIC ADVICE AND PAEDIATRIC INVESTIGATION PLAN (PIP)		
9. CONTENT OF THE LABELLING OF THE INVESTIGATIONAL MEDICINAL PRODUCTS		
10. RECRUITMENT ARRANGEMENTS		
11. SUBJECT INFORMATION, INFORMED CONSENT FORM AND INFORMED CONSENT PROCEDURE		
12. SUITABILITY OF THE INVESTIGATOR		
13. SUITABILITY OF THE FACILITIES		
14. PROOF OF INSURANCE COVER OR INDEMNIFICATION		
15. FINANCIAL AND OTHER ARRANGEMENTS		
16. PROOF THAT DATA WILL BE PROCESSED IN COMPLIANCE WITH UNION LAW ON DATA PROTECTION		
17. Other documents (please list and state which review body the document is for in the comments column. Documents which are for 'information only' should not be submitted but where such a document is submitted, this should be stated)		

Appendix 2

The following is a list of documents which do not need to be submitted. This list is being developed via the CWoW pilot and is not an exhaustive list.

- Separate covering letters for each of the IB's.
- Separate list of active trials (can be included in the cover letter)
- Raw data from viral validation studies.
- Literature references for quality data
- Additional documents confirming that another document was not required (e.g Scientific Advice (SAM) or a Paediatric Investigation Plan (PIP))
- UTN receipt
- EudraCT receipt
- EudraCT number confirmation
- Receipt of payment for MHRA review (the PO number should be included in the cover letter)

Section	Change	Version	Date
Throughout	To reflect the introduction of the new part of IRAS	3.7	21.4.20
Step 1, step 8 and types of trials excluded	ATIMP trials can be submitted under the pilot. We work towards the statutory timeframe of 90 days but aim to issue final outcomes within 60 days.	3.6	3.2.20
Figure 1 – application pack	Reference to submission of SSI form via IRAS removed	3.6	3.2.20
Steps 1 & 2	To reflect the revised process that trials should be registered with Cwow.admin@nhs.net but a REC and meeting date can only be confirmed once the applicant is confident they can submit with a stated submission period	3.4	7.10.19
Step 6	Confirming that correspondence will be sent to the contact e-mail supplied and it is the responsibility of the sponsor to ensure that the correspondence reaches the correct people. We also advise the use of generic rather than personal e-mail addresses.	3.4	7.10.19
Throughout	Remove the telephone numbers as e-mail communication is encouraged	3.4	7.10.19
Appendix 1 – document checklist	Addition of point 17 to add any other documents not listed and to state whether for REC or MHRA review or both.	3.4	7.10.19
Appendix 2	Addition of a list of documents which do not need to be submitted	3.4	7.10.19